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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,247	01/15/2004	Raymond A. Dwek	2543-1-023CON	5331

23565 7590 04/17/2006

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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,247	DWEK ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *4-8,12,13 and 16-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9-11,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is a First Office Action on the Merits of the Application filed 15 January 2004 as a continuation of 10/042,527 filed October 19, 2001, which is a Continuation of PCT/GB00/01560, filed April 20, 2000, which claims priority to United Kingdom Application 9909066.4, filed April 20, 1999. Claims 1-38, as originally filed, are pending.

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-15), N-butyldeoxynojirimycin (NB- DNJ) as the species of inhibitor of glycolipid synthesis degradation and Gaucher disease as the species of glycolipid storage-related disorder for initial examination in the reply filed 2 February 2006 is acknowledged.

Claims 16-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and claims 4-8, 12 and 13 are withdrawn as being drawn to non-elected species, there being no allowable generic or linking claim. Election was made **without** traverse in the 2 February reply.

Claims 1-3, 9-11, 14 and 15 are presently under consideration.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement filed 15 January 2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Specifically, no copy of the reference listed as AI has been filed and the reference also was not considered in the parent application 10/042,527. Copies of the other non-patent references are present in the parent application and have been considered.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 9-11, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In the instant case, the claims encompass a method for treating a glycolipid storage-related disorder comprising administering "an inhibitor of glycolipid synthesis" and compositions to be used in the claimed method which comprise said inhibitor of glycolipid synthesis. Therefore, the inhibitor of glycolipid synthesis is a critical element of both the method and composition. The Revised Interim Guidelines state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (Column 3, page 71434). Given its broadest reasonable interpretation, the limitation inhibitor of glycolipid synthesis encompasses a broad genus of any compound capable of inhibiting glycolipid synthesis in a cell. This genus would include inhibitors of enzymes involved in synthesis of more complex glycolipids, as well as crebroside, and inhibitors of enzymes that make the lipid and sugar substrates of the enzymes directly involved in glycolipid synthesis. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). The specification provides a detailed description reduction to practice of imido sugar compounds capable of inhibiting glucosylceramide synthase (see especially paragraph 51 and the Examples). The specification does not describe inhibitors of enzymes involved in synthesis of glycolipids other than glucosylceramide synthase. The specification fails to teach the chemical or physical

structures of inhibitors of enzymes other than glucosylceramide synthase or the common attributes of the genus of any compound capable of inhibiting glycolipid synthesis.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of *any* and *all* inhibitors of glycolipid synthesis. Therefore, only the described glucosylceramide synthase inhibitors meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1-3, 9-11, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing GSL in peripheral tissues comprising administering an inhibitor of glucosylceramide synthase in combination with a glucocerebrosidase enzyme or bone marrow transplantation, does not reasonably provide enablement for a method of treating a glycolipid storage-related disorder, as treatment is defined in the specification, comprising administering any inhibitor of glycolipid synthesis in combination with any agent capable of increasing the rate of glycolipid degradation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited

to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention: The invention contemplates treating glycolipid storage-related disorders using combination therapy, wherein an inhibitor of glycolipid synthesis and an agent capable of increasing glycolipid degradation are co-administered. Among the diseases contemplated in the specification are Gaucher disease, Sandhoff's disease, Fabry's disease and Tay-Sach's disease as well as Alzheimer's disease, stroke and epilepsy (see, e.g., claim 14). At paragraph 30, the specification defines "treatment" as "administration of medicine or the performance of medical procedures with respect to a patient, for either prophylaxis (prevention) or to cure the infirmity or malady in the instance where the patient is afflicted." According to this definition, the claims embrace a method of preventing or curing (*i.e.*, complete remission of all symptoms of the indicated diseases and the correction of the underlying genetic defect) any glycolipid storage disease, including Gaucher disease, Sandhoff's disease, Fabry's disease, Tay-Sach's disease, Alzheimer's disease, stroke and epilepsy, comprising administering any inhibitor of glycolipid synthesis in combination with any agent capable of increasing the rate of glycolipid degradation. It is also clear from the discussion of delivery options contemplated for the invention that the claims encompass gene therapy as a mode of treatment (see especially beginning at paragraph 56 and continued through paragraph 93).

State and level of predictability in the art: First, with regard to gene therapy, at the time of filing, *in vivo* gene therapy utilizing the direct administration of recombinant nucleic acids, whether in the form of retroviruses, adenoviruses, or plasmid DNA/liposome complexes, was considered to be highly unpredictable. Verma et al. states that, "[t]he Achilles heel of gene therapy is gene delivery...", and that, "most of the approaches suffer from poor efficiency of delivery and transient expression of the gene" (Verma et al. (1997) Science, Vol. 389, page 239, column 3, paragraph 2). Marshall concurs, stating that, "difficulties in getting genes transferred efficiently to target cells- and getting them expressed- remain a nagging problem for the entire field", and that, "many problems must be solved before gene therapy will be useful for more than the rare application" (Marshall (1995) Science, Vol. 269, page 1054, column 3, paragraph 2, and page 1055, column 1).

Orkin et al. further states in a report to the NIH that, "... none of the available vector systems is entirely satisfactory, and many of the perceived advantages of vector systems have not been experimentally validated", and that, "[w]hile the expectations and the promise of gene therapy are great, clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol" (Orkin et al. (1995) "Report and recommendations of the panel to assess the NIH investment in research on gene therapy", page 1, paragraph 3, and page 8, paragraph 2).

Among the many factors that the art teaches affect efficient gene delivery and sustained gene expression are, immune responses and the identity of the promoter used to drive gene expression. Verma et al. teaches that weak promoters produce only low levels of protein, and that only by using appropriate enhancer-promoter combinations can sustained levels of therapeutically effective protein expression be achieved (Verma et al., *supra*, page 240, column

2). Verma et al. further warns that, "... the search for such combinations is a case of trial and error for a given type of cell" (Verma et al., *supra*, page 240, bridging sentence of columns 2-3). The state of the art is such that no correlation exists between successful expression of a gene and a therapeutic result (Ross et al. Human gene Therapy, vol. 7, pages 1781-1790, September 1996, see page 1789, column 1, first paragraph).

In an article published well after the effective filing date of the instant application, Rubanyi (2001) *Mol. Aspects Med.* 22:113-142 teaches that the problems described above remained unsolved at the time the instant application was filed. Rubanyi states, "[a]lthough the theoretical advantages of [human gene therapy] are undisputable, so far [human gene therapy] has not delivered the promised results: convincing clinical efficacy could not be demonstrated yet in most of the trials conducted so far..." (page 113, paragraph 1). Among the technical hurdles that Rubanyi teaches remain to be overcome are problems with gene delivery vectors and improvement in gene expression control systems (see especially "**3. Technical hurdles to be overcome in the future**", beginning on page 116 and continued through page 125). Thus, the art at the time of filing clearly establishes that expectation for achieving a desired therapeutic effect *in vivo* by expressing a therapeutic gene using any of the expression constructs known in the art at the time of filing was extremely low.

With regard to agents capable of increasing the rate of glycolipid degradation administered by methods that to do not involve gene therapy, the art teaches treatment of type I Gaucher disease by administration of glucocerebrosidase or bone marrow transplantation (see especially Platt and Butters (1998; IDS AO) the sentence bridging columns 1 and 2 on page 424 and citations therein, and the first full paragraph on page 425). However, Platt and Butters

further teach that, "the major biological issue when considering enzyme replacement for the GSL storage disease is that the vast majority of these disorders, in contrast with type I Gaucher disease, have neurological phenotypes that result from GSL storage in cells of the CNS. Large glycoprotein enzymes do not cross the blood-brain barrier, and so this approach is only useful in diseases with systemic, non-CNS, storage...Also, this approach is disease specific, with each disease-specific enzyme requiring development for clinical evaluation" (page 425, paragraph 1). These teachings point out that, at the time of filing, the effective use of enzyme replacement, either alone or in combination with another agent, to treat a glycolipid storage-related disorder other than type I Gaucher disease was highly unpredictable. This is evidence by the lack of enzyme replacement therapy for a glycolipid storage-related disorder outside of type I Gaucher disease, the art recognized obstacle to development of enzyme replacement therapy for most glycolipid storage-related disorders created by the blood-brain barrier, and the recognition that success obtained with enzyme replacement therapy in the treatment of one glycolipid storage-related disorder cannot be generalized to other glycolipid storage-related disorders.

With regard to a method of treatment comprising administering an inhibitor of glycolipid synthesis wherein the primary target of said inhibitor of glycolipid synthesis is other than glucosylceramide synthase, the prior art does not provide teachings that would allow one of ordinary skill to practice the claimed invention using inhibitors of any enzyme involved in glycolipid synthesis. In fact, Aerts *et al.* (1998; IDS AH) teach that, "[a] disadvantage of the 'substrate deprivation' approach is that *a priori* not only the synthesis of glucosylceramide but also that of more complex glycosphingolipids is inhibited" (page 9, paragraph 1). This teaching indicates that inhibiting the synthesis of more complex glycosphingolipids is undesirable. In

view of such a teaching the skilled artisan would not predict that targeting enzymes involved in more complex glycosphingolipid synthesis would be effective in the claimed method.

Finally, with regard to preventing or curing diseases such as those listed in claim 14, the art does not recognize a single enabled method for preventing or curing any of the diseases. Therefore, the skilled artisan is fully dependent upon the teachings of the instant application for guidance as to how to prevent or cure the conditions.

Amount of direction provided by the inventor and existence of working examples: The disclosure provides examples of combined administration of the inhibitor of glycolipid synthesis NB-DNJ with two agents capable of increasing the rate of glycolipid degradation (i.e. Ceredase™ and transplanted bone marrow). The examples provided do not, however, remedy most of the deficiencies recognized in the art cited herein above. In the example of combined therapy comprising Ceredase™, applicants demonstrate only that the activity of Ceredase™ is not compromised by co-administration of NB-DNJ in normal mice and that co-administration of NB-DNJ appears to extend the half-life of Ceredase™. No evidence is provided to indicate that the combined therapy would be an effective treatment for all conditions of glycolipid storage-related disease, although one can speculate that the therapy could be developed for treatment of type I Gaucher disease, as Ceredase™ has been used successfully in the treatment of Gaucher disease in the past.

The findings of Example 3 (page 34) demonstrate that administration of NB-DNJ to a mouse model of Sandhoff disease following bone marrow transplantation significantly, and unexpectedly extended the survival of the Sandhoff mice beyond the survival of Sandhoff mice that received bone marrow transplantation alone. While these findings indicate that the

combination of bone marrow transplantation followed by administration of NB-DNJ can be used to delay mortality as a consequence of the defect associated with Sandhoff disease, they do not provide sufficient guidance, either alone or in combination with the teachings of the prior art, to enable one of ordinary skill to delay mortality as a consequence of any genetic defect other than the defect associated with Sandhoff disease, or to delay mortality as a consequence of the defect associated with Sandhoff disease through co-administration of NB-DNJ with any agent capable of increasing the rate of glycolipid degradation other than bone marrow transplantation.

Further, although the findings of Example 3, shows that the survival of Sandhoff mice could be extended by coadministration of NB-DNJ and bone marrow transplantation, the mice were by no means cured of the disease.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the level of skill in the art is high, the ordinary skilled artisan would not be able to make or use the invention commensurate with the scope of the claims without undue experimentation. The art recognizes a high degree of unpredictability in obtaining success using the methods of the instant Application. The reason for this unpredictability stems first from the lack of guidance as to how to use an agent capable of increasing the rate of glycolipid degradation outside of β-glucocerebrosidase or bone marrow transplantation, or how to use *any* agent administered by gene therapy; the lack of direction in the art with regard to how to effectively treat any glycolipid storage-related disease other than type I Gaucher disease using a method comprising an agent capable of increasing the rate of glycolipid degradation; and the art recognized barriers to generalizing success obtained in treating any given glycolipid storage-related disease to any other glycolipid storage-related disease. The teachings of the specification

remedy deficiencies in the art only with respect to delaying mortality as a consequence of the defect associated with Sandhoff disease by administering NB-DNJ following bone marrow transplantation. The skilled artisan would therefore have to engage in undue experimentation to extend these findings in order to practice the method of the elected invention over any scope beyond symptomatic relief in type I Gaucher disease by administration of an inhibitor of glucosylceramide synthase in combination with a glucocerebrosidase enzyme.

With regard to preventing or curing the elected Gaucher disease, prevention or cure would require correction of the underlying genetic defect as anything less would merely provide symptomatic relief. As correcting the genetic defect would require the successful application of gene therapy techniques, the claims are not fully enabled for the reasons set forth above.

In view of the foregoing, the skilled artisan would conclude that the claims are not enabled beyond the scope of a method of reducing GSL in the peripheral tissues comprising administering an inhibitor of glucosylceramide synthase in combination with a glucocerebrosidase enzyme or bone marrow transplantation. Therefore, the claims are properly rejected under 35 USC §112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation "the inhibitor of glucosylceramide synthesis" in line 1. There is insufficient antecedent basis for this limitation in claim 1, from which claim 2 depends. Claim 3 is indefinite insofar as it depends from claim 2.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would be obvious over, the reference claim(s).

Claims 1-3, 9-11, 14 and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 8 of U.S. Patent No. 6,696,059. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application merely broaden the scope of the claims of the cited Application.

To the extent that they are enabled by the disclosure, the claims of the instant application are drawn to a method of reducing GSL in the peripheral tissues comprising administering an

inhibitor of glucosylceramide synthase and a glucocerebrosidase enzyme. The claims of the '059 patent are directed to a method of treatment comprising administering to a patient a combination of both a N-alkyl derivative of deoxynojirimycin having from about two to about twenty carbon atoms in the alkyl chain and a glucocerebrosidase enzyme. Claim 8 limits the method to treatment of Gaucher disease. Thus, the enabled scope of the instant claims is generic to all that is recited in the claims of the conflicting patent. That is, the patented claims fall entirely within the scope of the instant claims. As the instant claims are anticipated by the patented claims, they cannot be viewed as patentably distinct therefrom. Therefore, the claims are properly rejected under the doctrine of nonstatutory double patenting.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Note: The following rejection applies to the extent that the prior art discloses the same method embraced by the instant invention. The prior art rejection is not to be construed as an indication that the claimed or anticipated methods are *enabled* for the breadth of subject matter potentially embraced by the claimed method of treatment. The compositions and/or methods disclosed in the prior art are essentially enabled to the same extent as the instant specification, since there is no significant difference in the level of guidance presented in either case.

Claims 1-3, 9-11, 14 and 15 are rejected under 35 U.S.C.§102(b) as being anticipated by any one of Platt *et al.* (1998; IDS AF), Platt and Butters (1998; IDS AO) or Aerts *et al.* (1998; IDS AH).

Claim 1, and claims 2, 3, 9-11, 14 and 15 as they depend from claim 1, are directed to a method for treating a glycolipid storage-related disorder, comprising administering a therapeutically effective amount of an inhibitor of glycolipid synthesis in combination with an agent capable of increasing the rate of glycolipid degradation.

Each of the cited references teach a method of treating glycolipid storage-related disorders comprising administering a an inhibitor of glycolipid synthesis (see especially Platt and Butters beginning the second paragraph on page 425 and continued through the second paragraph on page 428; Platt *et al.* beginning the fourth paragraph in column 1 and continued through the first paragraph in column 3; and Aerts *et al.* beginning the second full paragraph on page 8 and continuing through the first full paragraph on page 9). Each of the references then contemplates that the method of treating with an inhibitor of glycolipid synthesis can further comprise an agent capable of increasing the rate of glycolipid degradation (see especially Platt and Butters, the second full paragraph on page 425; Platt *et al.*, the final sentence of the first paragraph in column 3; and Aerts *et al.* page 39, claim 15).

Claim 2 is directed to the method of claim 1, wherein the inhibitor of [glycolipid synthesis] is an imido sugar; claim 3 is directed to the method of claim 2, wherein the imido sugar is N-butyldeoxynojirimycin (NB-DNJ); and claim 9 is dawn to the method of claim 1, wherein the inhibitor of glycolipid synthesis is an inhibitor of neuronal glycolipid synthesis.

Platt and Butters teach a method wherein the inhibitor of glycolipid synthesis can be NB-DNJ (see especially Figure 3, the caption thereto on page 426 and the list of abbreviations that appears as a footnote on page 421). Platt *et al.* teaches a method wherein the inhibitor of glycolipid synthesis is NB-DNJ (see especially "RESULTS" beginning in column 8, also see the

definition of DGJ in the second paragraph of column 1). Aerts *et al.* teaches a method wherein the inhibitor of glycolipid synthesis is butyl-deoxynogirimycin (see especially the second full paragraph on page 8). Thus, the cited art anticipates the limitations of claims 2, 3 and 9.

Claim 10 is drawn to the method of claim 1, wherein the agent capable of increasing the rate of glycolipid degradation is an enzyme involved in glycolipid degradation and claim 11 is directed to the method of claim 10, wherein the enzyme is glucocerebrosidase.

Each of the cited references teach the enzyme glucocerebrosidase (see especially Platt and Butters, *Enzyme Replacement Therapy* on page 425; Platt *et al.*, the final sentence of the first paragraph in column 3; and Aerts *et al.*, second full paragraph on page 5).

Claim 14 is directed to the method of claim l, wherein the glycolipid storage-related disorder is selected from the group consisting of Gaucher disease and claim 15 is directed to the method of claim 1, wherein the inhibitor of glycolipid synthesis and the agent capable of increasing the rate of glycolipid degradation are given simultaneously, sequentially, or separately.

Platt and Butters contemplates using the method to treat Gaucher disease (see especially Table I). Platt *et al.* also contemplates using the method to treat Gaucher disease (see especially the final sentence in the first paragraph of column 3) as does Aerts *et al.* (see especially claim 15 on page 39). Finally, as each of the cited references teach that the method should comprise co-administration of the inhibitor of glycolipid synthesis and the agent capable of increasing the rate of glycolipid degradation, one of ordinary skill would know that the method must comprise administering the agents simultaneously, sequentially or separately.

The method taught by each of Platt and Butters, Platt *et al.* and Aerts *et al.* is the same as the method taught in the instant application, therefore the limitations of the claims are anticipated by the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Daniel M. Sullivan, Ph.D.
Primary Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER